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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Rouli Zhou

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EXAMINER

GUSSOW, ANNE

ART UNIT

PAPER NUMBER

1643

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DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/540,539	<b>Applicant(s)</b> ZHOU ET AL.	
	<b>Examiner</b> ANNE M. GUSSOW	<b>Art Unit</b> 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,5-14 and 17-21 is/are pending in the application.
- 4a) Of the above claim(s) 7-11,14 and 17-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,5,6,12 and 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Claims 1 and 6 have been amended.  
Claims 3, 4, 15, and 16 have been cancelled.
2. Claims 7-11, 14, and 17-21 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 13, 2007.
3. Claims 1, 2, 5, 6, 12, and 13 are under examination.
4. The following office action contains NEW GROUNDS of Rejection.

### ***Rejections Withdrawn***

5. The rejection of claims 1-6, 12, 13, and 16 under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's amendment to the claims.

### ***NEW GROUNDS of Rejection***

#### ***Claim Objections***

6. Claims 12 and 13 are objected to because of the following informalities: the claims recite "vector of" and "cell lines of" respectively. The claims should read "vectors comprising" and "cell lines comprising". Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 2, 3, 6, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the cancer related nucleotide sequences of SEQ ID Nos. 1 and 6 and the cancer related polypeptide sequence of SEQ ID No. 4, does not reasonably provide enablement for all of the possible nucleotide sequences encoding SEQ ID No. 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,  
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to all possible cancer related nucleotide sequences that encode SEQ ID No. 4.

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The specification discloses the nucleotide sequence of SEQ ID No. 1 encodes SEQ ID No. 4 and is overexpressed in cancer. The specification does not disclose other degenerate nucleotide sequences which would encode SEQ ID No. 4 are associated with cancer. One of ordinary skill in the art would be forced into undue experimentation to determine which of the degenerate nucleotide sequence which encode SEQ ID No. 4 would be cancer related.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess, et al., Journal of Cell Biology, 1990. Vol. 111, pages 2129-2138, as cited in the office action mailed November 13, 2007). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar, et al. Molecular and Cellular Biology, 1988. Vol. 8 pages 1247-1252, as cited in the office action mailed November 13, 2007).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin (Schwartz, et al., Proceedings of the National Academy of Sciences, 1987. Vol. 84, pages 6408-6411, as cited in the office action mailed November 13, 2007). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate

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cyclase (Lin, et al. Biochemistry, 1975. Vol. 14, pages 1559-1563 as cited in the office action mailed November 13, 2007).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Even if one has the correct amino acid sequence, a skilled practitioner would not be able to predict the level of expression of the resulting synthetic DNA sequence. For example, the cellular location of the Int-2 oncoprotein is determined by the choice of initiation codon, i.e., either the AUG coding for methionine or CUG coding for leucine. AUG-initiated Int-2 proteins are secreted from the cells, while CUG-initiated Int-2 proteins are localized to the cell nucleus (Acland, et al., Nature 1990. Vol. 343, pages 662-665).

Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. Elucidation of the genetic code induces one to believe that one can readily obtain a functional synthetic protein for any known nucleic acid sequence with predictable results. The results of the construction of synthetic proteins remain very unpredictable as Burgess, et al., Lazar, et al., Schwartz, et al., Lin, et al. and Acland, et al. conclusively demonstrate.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

***Claim Rejections - 35 USC § 101***

9. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claim 13 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 13, as written, do not sufficiently distinguish over cells as they exist naturally because claim 13 does not particularly point out any non-naturally occurring differences between the claimed cells and the structure of naturally occurring cells.

In the absence of the hand of man, the naturally occurring cells are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" cell or similar language would obviate this rejection.

***Conclusion***

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is

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(571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow  
August 31, 2009

/Anne M Gussow/  
Examiner, Art Unit 1643